

# Sexual Abuse and Lifetime Diagnosis of Psychiatric Disorders: Systematic Review and Meta-analysis

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**OBJECTIVE:** To systematically assess the evidence for an association between sexual abuse and a lifetime diagnosis of psychiatric disorders.

**PATIENTS AND METHODS:** We performed a comprehensive search (from January 1980-December 2008, all age groups, any language, any population) of 9 databases: MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO, ACP Journal Club, CCTR, CDSR, and DARE. Controlled vocabulary supplemented with keywords was used to define the concept areas of sexual abuse and psychiatric disorders and was limited to epidemiological studies. Six independent reviewers extracted descriptive, quality, and outcome data from eligible longitudinal studies. Odds ratios (ORs) and 95% confidence intervals (CIs) were pooled across studies by using the random-effects model. The  $I^2$  statistic was used to assess heterogeneity.

**RESULTS:** The search yielded 37 eligible studies, 17 case-control and 20 cohort, with 3,162,318 participants. There was a statistically significant association between sexual abuse and a lifetime diagnosis of anxiety disorder (OR, 3.09; 95% CI, 2.43-3.94), depression (OR, 2.66; 95% CI, 2.14-3.30), eating disorders (OR, 2.72; 95% CI, 2.04-3.63), posttraumatic stress disorder (OR, 2.34; 95% CI, 1.59-3.43), sleep disorders (OR, 16.17; 95% CI, 2.06-126.76), and suicide attempts (OR, 4.14; 95% CI, 2.98-5.76). Associations persisted regardless of the victim's sex or the age at which abuse occurred. There was no statistically significant association between sexual abuse and a diagnosis of schizophrenia or somatoform disorders. No longitudinal studies that assessed bipolar disorder or obsessive-compulsive disorder were found. Associations between sexual abuse and depression, eating disorders, and posttraumatic stress disorder were strengthened by a history of rape.

**CONCLUSION:** A history of sexual abuse is associated with an increased risk of a lifetime diagnosis of multiple psychiatric disorders.

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CI = confidence interval; OR = odds ratio; PTSD = posttraumatic stress disorder

There is increasing recognition that many patients seen for general medical care have a history of sexual abuse. Prevalence rates of sexual abuse in the general population range from 4.0% to 21.4% in adults and from 3.0% to 33.2% in children.<sup>1-8</sup> Not surprisingly, sexual abuse survivors make up a sizable percentage (estimated at 13%-26%) of primary care practices.<sup>9-12</sup> In addition, these statistics are likely to be underestimates because of the frequent underreporting of sexual abuse.<sup>13,14</sup> The medical literature has long reported an association between sexual

abuse and psychiatric symptoms.<sup>15,16</sup> During the past 30 years, a number of clinical studies have attempted to investigate and better define the nature of this association. Recently, several systematic reviews have summarized data from these studies.<sup>17-20</sup> These reviews have reported an association between sexual abuse and depression, post-traumatic stress disorder (PTSD), eating disorders, and suicide attempts, but inclusion of cross-sectional studies limits the inferences drawn from the results. Furthermore, assessment of a narrow range of psychiatric conditions and limited subgroup analyses decrease the ability to generalize the results of these reviews.

To specifically address these limitations of previous studies, we conducted a comprehensive systematic review and meta-analysis to evaluate the available evidence for an association between sexual abuse and psychiatric disorders commonly encountered in general medical practice, including anxiety disorders, bipolar disorder, depression, eating disorders, obsessive-compulsive disorder, PTSD, schizophrenia, sleep disorders, somatoform disorders, and suicide attempts. The objective of the current study was to systematically assess and summarize the best available evidence of the association between a history of sexual abuse and a lifetime diagnosis of psychiatric disorders.

## PATIENTS AND METHODS

### DATA SOURCES AND SEARCHES

The protocol for this systematic review was developed by physicians and researchers in internal medicine, preventive medicine, epidemiology, statistics, and psychology. Methods described by the Cochrane Collaboration were used in the development of the protocol.<sup>21</sup> The reporting of results

From the Mayo Medical School (L.P.C., M.L.P., K.M.C., A.L.S., E.N.G.), Knowledge and Encounter Research Unit (M.H.M., M.B.E.), Division of Preventive, Occupational and Aerospace Medicine (M.H.M.), Department of Psychiatry and Psychology (R.J.S., G.S.), Mayo Clinic Libraries (L.J.P.), and Division of General Internal Medicine (A.Z.), Mayo Clinic, Rochester, MN. Dr Shinozaki is now with the VA Medical Center, Sioux Falls, SD.

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was based on the recommendations of the Meta-analysis of Observational Studies in Epidemiology group.<sup>22</sup>

We performed a comprehensive search (from January 1980–December 2008, all age groups, any language, any population) of 9 databases: MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO, ACP Journal Club, CCTR, CDSR, and DARE. The search strategy was designed and conducted by an experienced librarian (L.J.P.) with input from the study's principal investigator (A.Z.). Controlled vocabulary supplemented with keywords was used to define the concept areas of sexual abuse and psychiatric disorders and was limited to epidemiological studies. Additional details are available from the corresponding author.

### STUDY SELECTION

Eligible studies were longitudinal observational studies (case-control and cohort) that compared individuals who had a history of sexual abuse with a control group. Foreign-language articles and unpublished research were included.

Sexual abuse exposure was categorized into 2 groups: *rape* and *all forms of sexual abuse*. *Rape* was defined as penetration (vaginal, anal, or oral) with a body part or foreign object. *All forms of sexual abuse* included a wide variety of definitions characterizing sexual violence (including, but not limited to, noncontact exposure of genitalia, threatened sexual violence, and contact involving genitalia and the mouth).<sup>23</sup> If studies included data for sexually abused, physically abused, and nonabused subjects, the 2 last-mentioned groups were pooled as controls.

Outcomes included anxiety disorders (generalized anxiety disorder, social phobias, specific phobias, panic disorders, agoraphobia, and anxiety disorders not otherwise specified), bipolar disorder, depression, eating disorders (anorexia nervosa and bulimia nervosa), obsessive-compulsive disorder, PTSD, schizophrenia, sleep disorders (night terrors, insomnia, narcolepsy, and sleep disorders not otherwise specified), somatoform disorders (conversion, somatization, hypochondriasis, and body dysmorphic disorders), and suicide attempts.

We contacted authors for data if the study appeared eligible on the basis of article review but the required data were unpublished, or if the study was published in a language for which we had no available translator. Requests for data were made by electronic mail or letters.

### DATA EXTRACTION

Reviewers (L.P.C., M.L.P., K.M.C., A.L.S., E.N.G., and A.Z.) worked independently and in duplicate to analyze eligible titles, abstracts, and full-text articles. Data were extracted in duplicate. Reviewers obtained study descriptions, including detailed information regarding study participants

(mean age, sex, and race). If greater than 70% of the study population was of one race, the study was designated as evaluating that race predominantly. Otherwise, the study was noted as evaluating a mixed-race population. Scandinavian studies were assumed to enroll predominantly white participants. Reviewers recorded the type of sexual abuse (either rape or all forms of sexual abuse). Childhood abuse was defined as abuse occurring at or before age 18 years.

Raw data for the exposed, nonexposed, outcome, and nonoutcome groups were obtained if possible. If raw numbers were not available, summary data of odds ratios (ORs) and 95% confidence intervals (CIs) were used, with preference given to the adjusted OR. Data extraction was re-examined by a second reviewer for accuracy. Authors of eligible articles not presenting raw data or ORs were contacted by electronic mail or letters and asked to provide data not printed in the published article.

### QUALITY ASSESSMENT

The quality of each eligible study was assessed in duplicate. The Newcastle-Ottawa quality assessment scale was used for case-control and cohort studies.<sup>24</sup> This scale consists of 8 questions and gives a maximum of 10 possible points for each type of study.

### STATISTICAL ANALYSES

Odds ratios were pooled for dichotomous outcomes from each study by using the DerSimonian-Laird random-effects model.<sup>25</sup> The 95% CI for each outcome was estimated to reflect the uncertainty of point estimates of effect.

An OR of 1.0 indicates no association, and an OR greater than 1.0 indicates increased risk for the referenced outcome. The  $I^2$  statistic was used to estimate the percentage of total variation across studies because of heterogeneity rather than chance (ie, the percentage of variability of associations across studies that is not due to chance or random error, but rather is due to real differences in study patients, design, or outcome definitions).  $I^2$  values of less than or equal to 25%, 50%, and greater than or equal to 75% represent low, moderate, and high levels of heterogeneity, respectively.<sup>26</sup> Statistical analysis was conducted using Comprehensive Meta-analysis Version 2 (Biostat, Englewood, NJ).<sup>27</sup>

A priori hypotheses were developed to explore subgroup interactions and to explain inconsistency in the direction and magnitude of associations among studies. These included study design (cohort vs case-control), age at which sexual abuse occurred (childhood vs adult), and sex and race of the abuse survivor.

To test a subgroup effect, we used a test of interaction<sup>28</sup> with a predetermined 2-tailed  $\alpha$  of .05. Subgroup analyses in meta-analyses are considered hypothesis-generating

rather than hypothesis-testing. Therefore, we did not make adjustments for multiple comparisons. We conducted a sensitivity analysis to determine whether the type of abuse (rape vs all forms of sexual abuse) or the statistical methods (random-effects model vs fixed-effect model) would alter study conclusions.

To assess the potential effect of publication bias, we planned to visually inspect funnel plots for asymmetry and use the Duval and Tweedie trim-and-fill method and the Begg and Mazumdar rank correlation test.

## RESULTS

### STUDY CHARACTERISTICS

This systematic review yielded 37 studies, 17 case-control and 20 cohort, with 3,162,318 participants (Figure 1).<sup>7,29-64</sup> Twenty-seven studies assessed childhood abuse, one study assessed adult abuse, and 2 studies assessed adult and childhood abuse separately. The remaining 7 studies did not stratify or report the age at which abuse occurred. Sixteen studies assessed female victims, one study assessed male victims, and 20 studies assessed both male and female victims. Twenty studies were conducted in countries

outside the United States. No foreign-language articles or unpublished work met criteria for inclusion. Additional study characteristics can be found in eAppendix (online linked to this article).

### STUDY QUALITY

None of the studies fulfilled all the Newcastle-Ottawa quality criteria. Of 17 case-control studies, 11 enrolled cases and controls from the same study population, and 10 studies matched exposed and nonexposed individuals. Only 3 of the case-control studies ascertained sexual abuse exposure by a secure record. Of the 20 cohort studies, 13 included exposed groups representative of the community. Only 4 studies ascertained the outcome by a secure record. Further details regarding study quality for case-control and cohort studies can be found in Tables 1 and 2, respectively.

### META-ANALYSES

A significant association was found between a history of sexual abuse and a lifetime diagnosis of anxiety disorders (OR, 3.09; 95% CI, 2.43-3.94), depression (OR, 2.66; 95% CI, 2.14-3.30), eating disorders (OR, 2.72; 95% CI, 2.04-

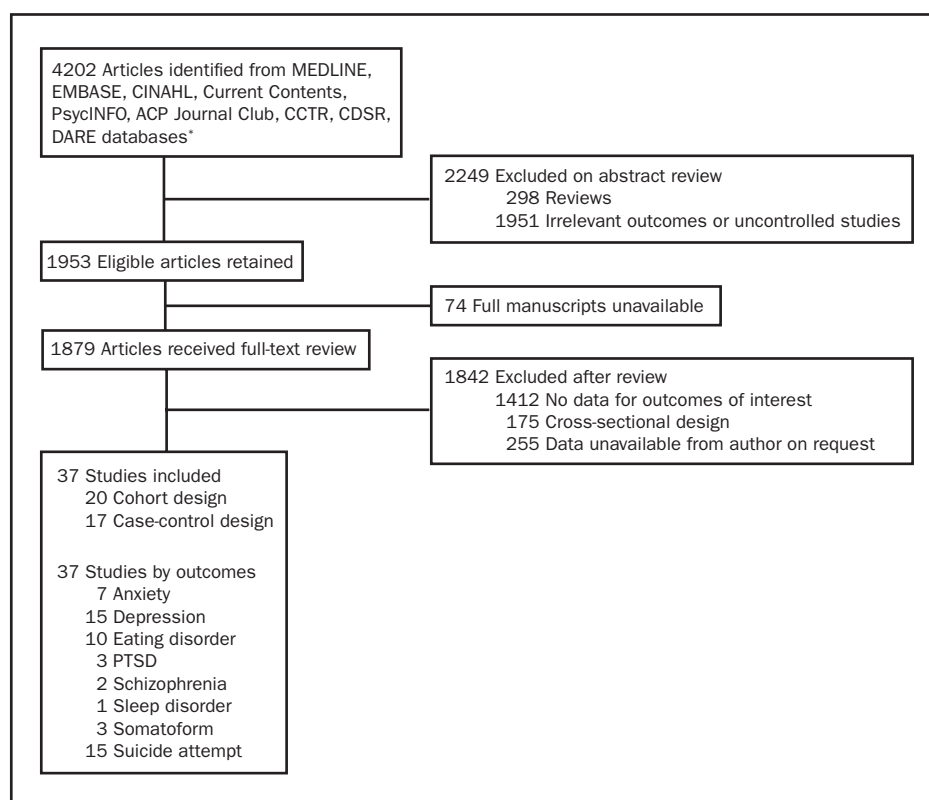


FIGURE 1. Literature search and study selection process. PTSD = posttraumatic stress disorder.

\* Literature search included somatic outcomes reported elsewhere.

TABLE 1. Quality Assessment for Case-Control Studies Using Newcastle-Ottawa Scale (n=17)

| Reference                                | Independent validation of cases | Appropriately selected cases must meet all 4 criteria <sup>a</sup> | Controls from same population as cases | Explicit statement controls have no history of outcome | Exposed and nonexposed individuals |                          |                                       | Exposure ascertained by                |                            | Same method of ascertaining cases and controls | Response rates same for cases and controls |
|--|---------------------------------|--|--|--|------------------------------------|--------------------------|---------------------------------------|--|----------------------------|--|--|
|  |                                 |  |  |  | Matched                            | Matched by second factor | Adjusted by 1 factor when no matching | Adjusted by >1 factor when no matching | Secure record (chart/file) | Structured interview <sup>b</sup>              |  |
| Brown et al, <sup>32</sup> 1997          |                                 | Yes  |  |  |                                    |                          |                                       |  |                            | Yes  |  |
| Cachelin et al, <sup>34</sup> 2005       |                                 | Yes  | Yes                                    |  |                                    |                          |                                       |  |                            | Yes  |  |
| Cheasty et al, <sup>7</sup> 1998         |                                 | Yes  | Yes                                    |  |                                    |                          |                                       |  |                            | Yes  |  |
| De Bellis et al, <sup>37</sup> 1994      |                                 |  |  |  | Yes                                | Yes                      |                                       |  | Yes                        |  |  |
| Deep et al, <sup>38</sup> 1999           |                                 |  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            | Yes  |  |
| Figueroa et al, <sup>44</sup> 1997       |                                 |  |  |  |                                    |                          |                                       |  |                            | Yes  | Yes  |
| Garnefski et al, <sup>47</sup> 1992      |                                 | Yes  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Pettigrew & Burcham, <sup>51</sup> 1997  |                                 |  | Yes                                    | Yes  |                                    |                          |                                       |  | Yes                        |  |  |
| Price et al, <sup>53</sup> 2002          |                                 | Yes  | Yes                                    |  | Yes                                |                          |                                       |  | Yes                        | Yes  |  |
| Roelofs et al, <sup>55</sup> 2002        |                                 | Yes  |  |  | Yes                                | Yes                      |                                       |  |                            | Yes  | Yes  |
| Spitzer et al, <sup>57</sup> 2008        |                                 | Yes  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Steiger et al, <sup>58</sup> 2000        |                                 |  |  | Yes  |                                    |                          |                                       |  |                            |  | Yes  |
| Striegel-Moore et al, <sup>59</sup> 2002 |                                 | Yes  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Stuart et al, <sup>60</sup> 1990         |                                 |  |  | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Tanskanen et al, <sup>61</sup> 2004      |                                 | Yes  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Welch & Fairburn, <sup>62</sup> 1996     |                                 | Yes  | Yes                                    | Yes  | Yes                                | Yes                      |                                       |  |                            |  | Yes  |
| Wise et al, <sup>64</sup> 2001           | Yes                             | Yes  | Yes                                    |  |                                    |                          |                                       |  |                            |  | Yes  |

<sup>a</sup> Criteria: (1) during defined period; (2) during defined area; (3) all cases in a defined group; (4) appropriate sample (random or consecutive).

<sup>b</sup> With blinding to measured outcome.

3.63), PTSD (OR, 2.34; 95% CI, 1.59-3.43), sleep disorders (OR, 16.17; 95% CI, 2.06-126.76), and suicide attempts (OR, 4.14; 95% CI, 2.98-5.76).

No statistically significant association was found between a history of sexual abuse and a lifetime diagnosis of schizophrenia (OR, 1.36; 95% CI, 0.81-2.30) or somatoform disorders (OR, 1.90; 95% CI, 0.81-4.47). We found no eligible longitudinal studies that assessed the outcomes of bipolar disorder or obsessive-compulsive disorder. The results are summarized in Table 3, and further details may be found in Figures 2 through 9.

#### SUBGROUP ANALYSES AND HETEROGENEITY

We found no significant subgroup-effect interactions based on the sex of the abused or the age of the victim at the time of abuse (Table 4). Data were insufficient to

conduct subgroup analyses for the outcomes of PTSD, somatoform disorders, or sleep disorders. Marked heterogeneity ( $I^2$  value >50%) was present in the analyses of depression and suicide attempts. Subgroup analyses of those statistically significant outcomes did not fully explain heterogeneity.

#### SENSITIVITY ANALYSIS

To determine the effect of the severity of sexual abuse, we performed a sensitivity analysis. A history of rape was found to strengthen the association with lifetime diagnoses of depression (OR, 6.27; 95% CI, 1.96-20.06; 2 studies), eating disorders (OR, 21.69; 95% CI, 1.26-373.39; one study), and PTSD (OR, 2.57; 95% CI, 1.13-5.87; one study). We did not find a history of rape to be associated with a lifetime diagnosis of somatoform disorders (one

TABLE 2. Quality Assessment for Cohort Studies Using Newcastle-Ottawa Scale (n=20)

| Reference                             | Exposed group representative of average in community | Exposure ascertained through structured records or structured interviews | Nonexposed group selected randomly or consecutively from population | Outcome not present at study start | Exposed and nonexposed individuals |                           |                            | Outcome ascertained by independent or blind assessment | Outcome conformation via secure record (chart/file) | Follow-up time long enough for outcome to occur | Lost to follow-up <20% |
|---------------------------------------|--|--|---|------------------------------------|------------------------------------|---------------------------|----------------------------|--|---|---|------------------------|
|                                       |  |  |   |                                    | Matched by second factor           | Adjusted by               | Adjusted by                |  |   |   |                        |
|                                       |  |  |   |                                    |                                    | 1 factor when no matching | >1 factor when no matching |  |   |   |                        |
| Aglan et al, <sup>29</sup> 2008       |  | Yes  |   |                                    |                                    |                           |                            |  |   | Yes   | Yes                    |
| Brezo et al, <sup>30</sup> 2008       | Yes  |  |   |                                    |                                    |                           | Yes                        |  |   | Yes   |                        |
| Brown et al, <sup>31</sup> 1999       | Yes  | Yes  | Yes   |                                    |                                    |                           | Yes                        |  |   |   |                        |
| Buist & Janson, <sup>33</sup> 2001    |  | Yes  |   |                                    |                                    |                           |                            | Yes  |   | Yes   | Yes                    |
| Chowdhary & Patel, <sup>36</sup> 2008 | Yes  | Yes  | Yes   |                                    |                                    |                           | Yes                        |  |   | Yes   | Yes                    |
| Dinwiddie et al, <sup>39</sup> 2000   | Yes  | Yes  |   |                                    |                                    | Yes                       |                            |  |   | Yes   |                        |
| Ernst et al, <sup>40</sup> 1993       | Yes  | Yes  |   |                                    |                                    |                           |                            |  |   | Yes   |                        |
| Fergusson et al, <sup>42</sup> 2000   | Yes  | Yes  | Yes   |                                    |                                    |                           |                            |  |   | Yes   |                        |
| Fergusson et al, <sup>43</sup> 2002   | Yes  |  | Yes   | Yes                                |                                    |                           |                            |  |   | Yes   | Yes                    |
| Fergusson et al, <sup>41</sup> 2008   | Yes  | Yes  |   |                                    |                                    |                           |                            | Yes  |   | Yes   |                        |
| Fiorentine et al, <sup>45</sup> 1999  |  | Yes  | Yes   |                                    |                                    |                           |                            |  |   | Yes   |                        |
| Frank & Anderson, <sup>46</sup> 1987  | Yes  | Yes  |   |                                    | Yes                                |                           |                            |  |   | Yes   | Yes                    |
| Gutner et al, <sup>48</sup> 2006      | Yes  | Yes  | Yes   |                                    |                                    |                           |                            |  |   | Yes   | Yes                    |
| Harvey et al, <sup>49</sup> 1994      |  | Yes  |   |                                    |                                    |                           |                            |  |   | Yes   | Yes                    |
| Kolko et al, <sup>50</sup> 2003       |  | Yes  |   |                                    |                                    |                           |                            | Yes  | Yes   | Yes   | Yes                    |
| Pearce et al, <sup>35</sup> 2008      |  | Yes  |   |                                    |                                    |                           | Yes                        |  |   | Yes   |                        |
| Plunkett et al, <sup>52</sup> 2001    | Yes  | Yes  | Yes   | Yes                                |                                    |                           |                            |  |   | Yes   |                        |
| Rimsza et al, <sup>54</sup> 1988      |  | Yes  | Yes   | Yes                                | Yes                                | Yes                       |                            |  | Yes   | Yes   | Yes                    |
| Spataro et al, <sup>56</sup> 2004     | Yes  | Yes  | Yes   |                                    |                                    |                           |                            | Yes  | Yes   | Yes   |                        |
| Widom, <sup>63</sup> 1999             | Yes  | Yes  | Yes   |                                    | Yes                                | Yes                       |                            | Yes  | Yes   | Yes   |                        |

study). No data were available to conduct sensitivity analysis for the other outcomes.

The use of the fixed-effect model did not change study conclusions regarding the outcomes that were nonsignificant under the random-effects model. As a result, we thought that the current analysis was robust, and we would not predict conclusions to be altered by changes in the choice of statistical model.

#### PUBLICATION BIAS

The inspection of funnel plots and the statistical tests for publication bias did not reveal an obvious effect of publication bias.

TABLE 3. Summary of Outcomes<sup>a</sup>

| Outcome                       | No. of studies | OR (95% CI) <sup>b</sup> | I <sup>2</sup> <sup>c</sup> | P value |
|-------------------------------|----------------|--------------------------|-----------------------------|---------|
| Anxiety disorders             | 8              | 3.09 (2.43-3.94)         | 40                          | .001    |
| Depression                    | 16             | 2.66 (2.14-3.30)         | 57                          | .001    |
| Eating disorders              | 11             | 2.72 (2.04-3.63)         | 20                          | .001    |
| Posttraumatic stress disorder | 3              | 2.34 (1.59-3.43)         | 0                           | .001    |
| Schizophrenia                 | 3              | 1.36 (0.81-2.30)         | 0                           | .45     |
| Sleep disorders               | 1              | 16.17 (2.06-126.76)      | NA                          | .01     |
| Somatoform disorders          | 3              | 1.90 (0.81-4.47)         | 4                           | .17     |
| Suicide attempts              | 19             | 4.14 (2.98-5.76)         | 60                          | .001    |

<sup>a</sup> CI = confidence interval; NA = not applicable; OR = odds ratio.

<sup>b</sup> All meta-analyses were performed using random-effects models.

<sup>c</sup> I<sup>2</sup> values of <25%, 50%, and >75% represent low, moderate, and high levels of heterogeneity, respectively.

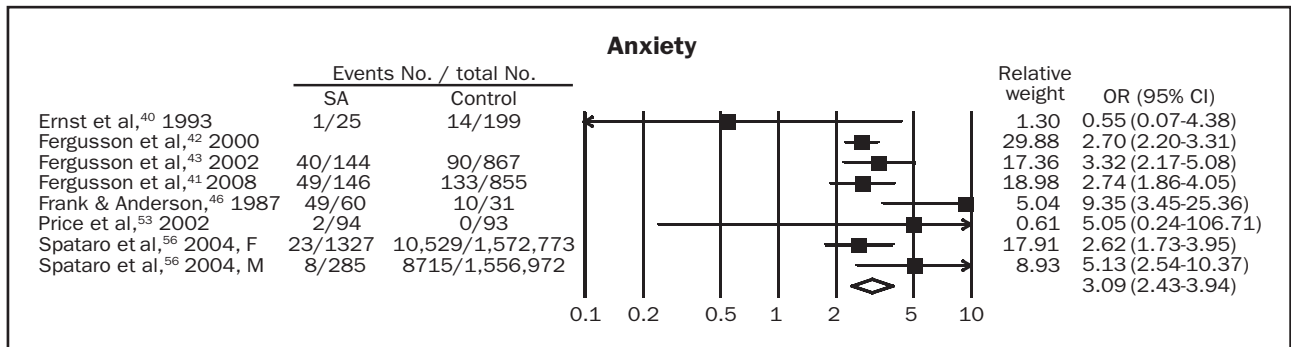


FIGURE 2. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of anxiety. CI = confidence interval; F = female; M = male.

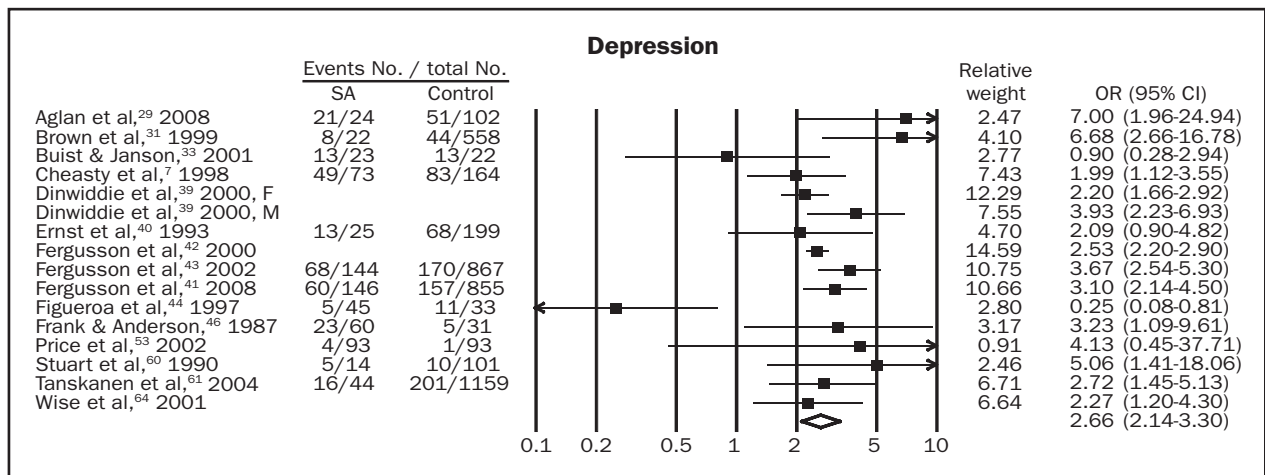


FIGURE 3. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of depression. CI = confidence interval; F = female; M = male.

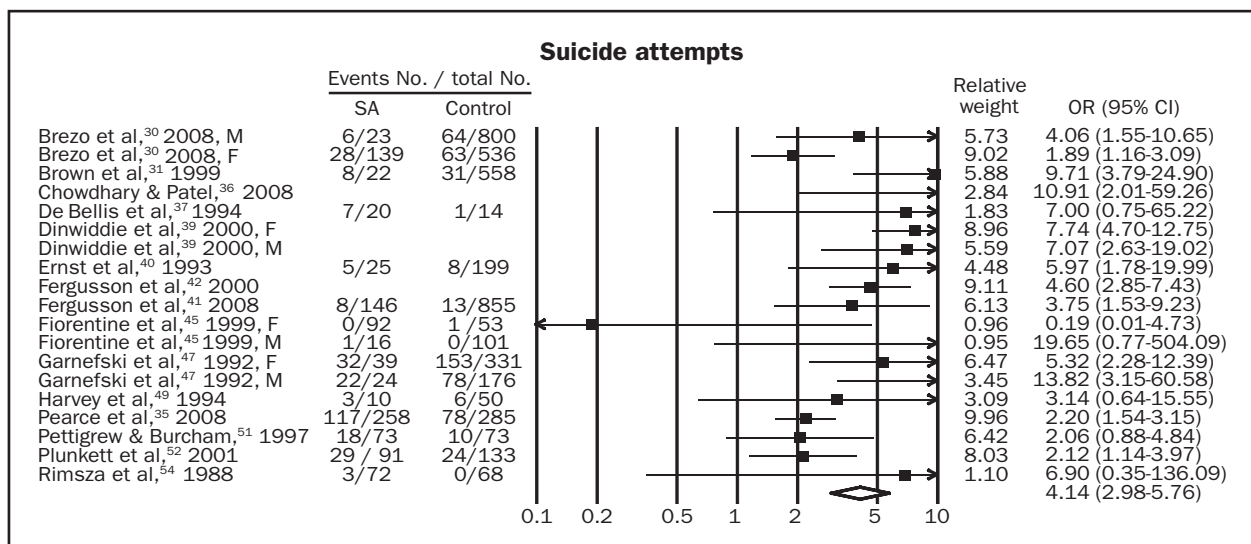


FIGURE 4. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of suicide attempts. CI = confidence interval; F = female; M = male.

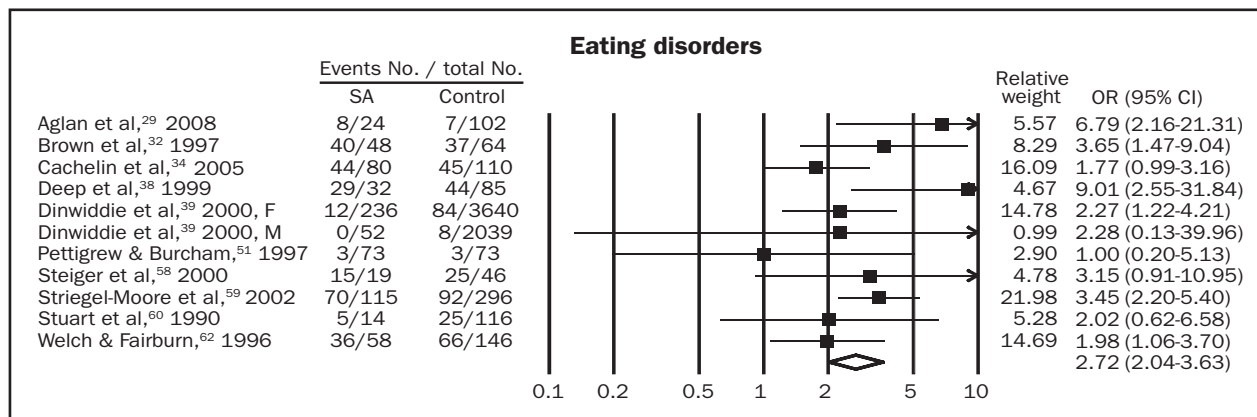


FIGURE 5. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of eating disorders. CI = confidence interval; F = female; M = male.

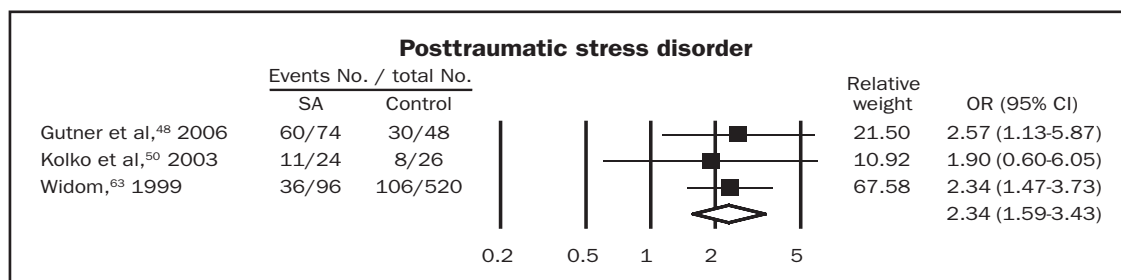


FIGURE 6. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of posttraumatic stress disorder. CI = confidence interval.

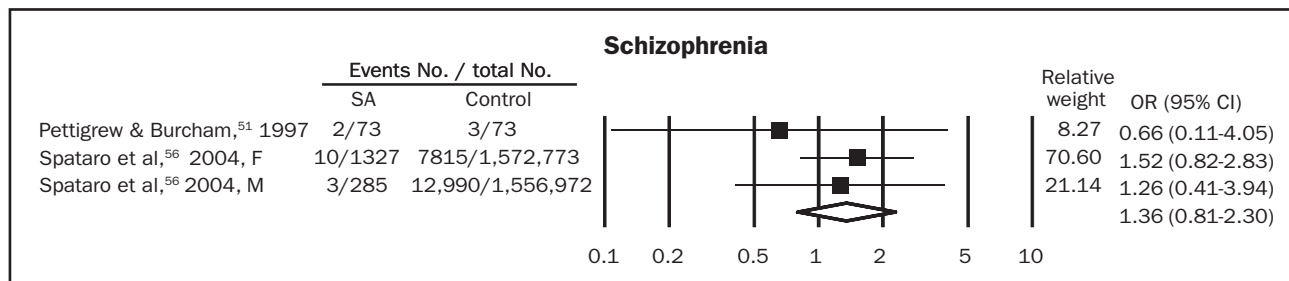


FIGURE 7. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of schizophrenia. CI = confidence interval; F = female; M = male.

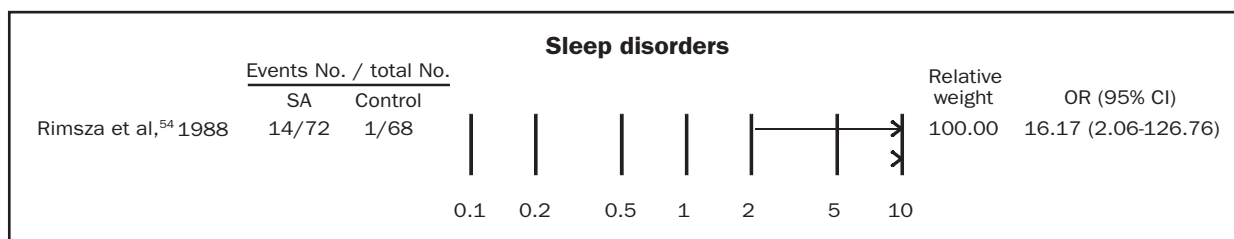


FIGURE 8. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of sleep disorders. CI = confidence interval.

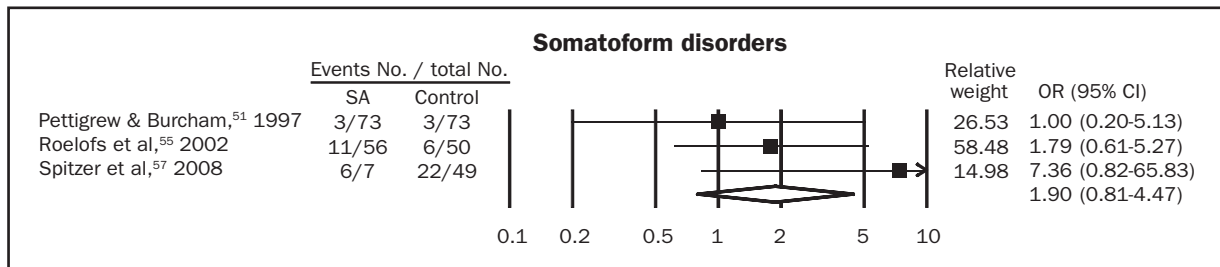


FIGURE 9. Odds ratio (OR) of the association between sexual abuse (SA) and lifetime diagnosis of somatoform disorders. CI = confidence interval.

TABLE 4. Subgroup Analysis<sup>a</sup>

| Outcome/<br>subgroup <sup>b</sup> | No. of<br>studies | OR (95% CI)        | I <sup>2</sup><br>(%) | P<br>interaction |
|-----------------------------------|-------------------|--------------------|-----------------------|------------------|
| <b>Anxiety</b>                    |                   |                    |                       |                  |
| Females                           | 3                 | 3.58 (1.90-6.76)   | 63                    | .56              |
| Males                             | 2                 | 5.12 (1.85-14.17)  | NA                    |                  |
| Childhood<br>abuse                | 8                 | 2.82 (2.43-3.27)   | 0                     | .05              |
| Adult abuse                       | 1                 | 7.21 (2.81-18.51)  | NA                    |                  |
| Case-control<br>design            | 1                 | 5.05 (0.23-109.93) | NA                    | .76              |
| Cohort design                     | 7                 | 3.10 (2.41-4.00)   | 48                    |                  |
| <b>Depression</b>                 |                   |                    |                       |                  |
| Females                           | 6                 | 2.20 (1.76-2.75)   | 0                     | .05              |
| Males                             | 2                 | 3.94 (2.28-6.83)   | NA                    |                  |
| Childhood<br>abuse                | 14                | 2.62 (2.10-3.26)   | 59                    | .05              |
| Adult abuse                       | 1                 | 8.87 (2.75-28.66)  | NA                    |                  |
| Case-control<br>design            | 6                 | 2.00 (1.31-3.05)   | 68                    | .12              |
| Cohort design                     | 10                | 2.95 (2.29-3.82)   | 48                    |                  |
| <b>Eating disorders</b>           |                   |                    |                       |                  |
| Females                           | 8                 | 2.34 (1.70-3.20)   | 10                    | .99              |
| Males                             | 1                 | 2.28 (0.13-40.53)  | NA                    |                  |
| Case-control<br>design            | 8                 | 2.65 (1.87-3.77)   | 28                    | .70              |
| Cohort design                     | 3                 | 3.08 (1.58-6.01)   | 27                    |                  |
| <b>Schizophrenia</b>              |                   |                    |                       |                  |
| Females                           | 2                 | 1.39 (0.77-2.51)   | NA                    | .88              |
| Males                             | 1                 | 1.26 (0.41-3.94)   | NA                    |                  |
| Case-control<br>design            | 1                 | 0.66 (0.11-4.05)   | NA                    | .41              |
| Cohort design                     | 2                 | 1.46 (0.84-2.52)   | NA                    |                  |
| <b>Suicide attempts</b>           |                   |                    |                       |                  |
| Females                           | 8                 | 3.24 (1.90-5.53)   | 71                    | .13              |
| Males                             | 4                 | 7.20 (3.01-17.22)  | 0                     |                  |
| Childhood<br>abuse                | 14                | 3.85 (2.75-5.40)   | 93                    | .30              |
| Adult abuse                       | 1                 | 10.91 (1.60-74.48) | NA                    |                  |
| Case-control<br>design            | 4                 | 4.71 (2.15-10.36)  | 47                    | .73              |
| Cohort design                     | 15                | 4.04 (2.78-5.87)   | 64                    |                  |
| White race                        | 5                 | 3.89 (2.00-7.58)   | 58                    | .40              |
| Native<br>American                | 1                 | 2.20 (0.70-6.96)   | NA                    |                  |

<sup>a</sup> CI = confidence interval; NA = not applicable; OR = odds ratio.

<sup>b</sup> Only feasible analyses are shown; no data were available for subgroup analyses on the outcomes of posttraumatic stress disorder, somatoform disorders, or sleep disorders.

## DISCUSSION

This comprehensive systematic review and meta-analysis of 37 longitudinal observational comparative studies including 3,162,318 participants found an association between a history of sexual abuse and a lifetime diagnosis of anxiety, depression, eating disorders, PTSD, sleep disorders, and suicide attempts. There was no statistically significant association between a history of sexual abuse and a lifetime diagnosis of schizophrenia or somatoform disorders. Association between sexual abuse and psychiatric disorders persisted regardless of sex of the abuse survivor or age at which abuse occurred. History of rape strengthened the associations between history of abuse and depression, eating disorders, and PTSD. No data were available to assess the outcomes of bipolar or obsessive-compulsive disorder.

Analyses appeared robust with regard to the statistical model and were associated with a low level of heterogeneity. Exceptions included the outcomes of depression and suicide attempts. Residual unexplained heterogeneity may be attributable to other study-level or patient-level covariates that could not be evaluated in this meta-analysis.

Using methodology similar to that in our current study, we recently conducted a systematic review and meta-analysis that found an association between a history of sexual abuse and several somatic disorders, including functional gastrointestinal disorders, chronic pelvic pain, psychogenic seizures, and nonspecific chronic pain.<sup>65</sup> Taken together with the results presented in the current meta-analysis, these findings lead us to conclude that a number of psychiatric and somatic disorders are associated with a history of sexual abuse. Many of these associations persist regardless of the age at which the sexual abuse occurred or the sex of the abuse survivor. Furthermore, some of the associations are strengthened by the occurrence of rape.

Several other meta-analyses have assessed the association of sexual abuse and psychiatric outcomes. Paolucci et al<sup>19</sup> reviewed published and unpublished research from 1981 to 1995 to assess the link between childhood sexual abuse and depression, PTSD, and suicide. The authors found a

significant association between childhood sexual abuse and depression, PTSD, and suicide, even after adjustment for socioeconomic status, type of abuse, relationship to abuser, and number of abuse episodes. Other systematic reviews have focused on individual diagnoses from the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition). In 1995, Jumper<sup>18</sup> conducted a meta-analysis including adults with a history of childhood sexual abuse and demonstrated an association between childhood sexual abuse and depression. In 1999, Fossati et al<sup>66</sup> found no association between childhood sexual abuse and borderline personality disorder in a review of observational studies. In 2002, Smolak and Murnen<sup>20</sup> conducted a meta-analysis of 53 studies and described an association between childhood sexual abuse and eating disorders.

More recently, Gilbert et al<sup>17</sup> performed a systematic review of longitudinal studies of childhood maltreatment and mental health outcomes between 2000 and 2008. This study found an association between childhood maltreatment and depression, PTSD, and suicide attempts. However, the authors did not perform a meta-analysis specific for the association of sexual abuse and mental health outcomes.

Our study builds on the previous literature and expands on prior systematic reviews by updating and presenting the best available evidence for the association between a history of sexual abuse and psychiatric disorders most commonly encountered in general medical practice. Previous study searches were limited to fewer databases and explored reference lists, whereas we performed a comprehensive, systematic search of 9 databases. Our review was also more temporally inclusive, searching articles from 1980 to 2008. Other reviews were limited by focusing solely on childhood abuse and by including a few psychiatric diagnoses. We expanded the scope to include both childhood and adulthood sexual abuse and their association with 10 common psychiatric disorders. In addition, we performed subgroup analyses based on the victim's race, sex, and age at which abuse occurred, as well as a sensitivity analysis for rape. Also, in contrast to previous systematic reviews, we excluded cross-sectional studies from our analysis. Such studies are prone to quality-of-evidence problems, and their results cannot infer causality.

Important strengths of the current study are its comprehensive and reproducible search strategy and its exhaustive selection process. Furthermore, we attempted to decrease bias by performing data extraction in pairs of independent reviewers and by communicating with authors of original studies to obtain unpublished or incomplete data. Efforts were made to evaluate foreign-language and unpublished studies.

The main limitation of the current study is the use of data susceptible to bias. No studies met all the Newcastle-Ottawa

criteria for study quality. Only 6 of 37 studies fulfilled more than half of the criteria. Among case-control studies, only Wise et al<sup>64</sup> provided independent validation of cases. All other studies used self-reporting from questionnaires or interviews. Notably, self-reporting in case-control studies may lead to recall bias. As an example, self-reporting of childhood sexual abuse is thought to lead to significant underreporting. Previous studies show significant variability in the percentage of documented survivors (62%-81%) who recall the abuse as adults.<sup>67-69</sup> The effect of underreporting would be to include survivors of sexual abuse in the control group, potentially decreasing the effect size of the association between abuse and psychiatric outcomes.

Attempts were also made to minimize publication bias by requesting unpublished data in the form of graduate-level theses and dissertations, conference abstracts, and foreign-language studies. However, no unpublished studies met eligibility criteria. Although review of funnel plots showed no obvious publication bias, the impact of such bias remains difficult to measure.<sup>70</sup>

In addition, previous research has shown that emotional, physical, and sexual abuse tend to coexist.<sup>71,72</sup> In the current review, only 18 of 37 studies assessed multiple categories of abuse, including physical and verbal violence. Thus, sexual abuse survivors may also have been exposed to other types of abuse, which may have affected the observed association.

No well-validated theory currently exists to explain the association between a history of sexual abuse and psychiatric outcomes. However, growing evidence supports the hypothesis of a gene-environment interaction in which genetic vulnerability alters an individual's ability to respond to stress. The serotonin transporter gene and its association with depression have been the focus of many such studies. Original work by Caspi et al<sup>73</sup> in a large New Zealand birth cohort demonstrated that people homozygous for the short form of the serotonin transporter gene promoter region polymorphism (*5HTTLPR*) are at higher risk of depression than people with other genotypes if they experience childhood maltreatment. The study also demonstrated that people homozygous for the long form of *5HTTLPR* who have a history of childhood maltreatment are at lower risk of developing depression than people with other genotypes. This result was replicated by many additional independent studies, including work by Kendler et al.<sup>74</sup> Kaufman et al<sup>75</sup> demonstrated that *5HTTLPR* and brain-derived neurotrophic factor (*BDNF*) gene polymorphisms interact to increase the severity of depression in children exposed to adverse events. Another study also demonstrated the interaction between *5HTTLPR* and catechol O-methyltransferase (*COMT*) in increasing the risk of depression.<sup>76</sup> However, a recent meta-analysis of the *5HTTLPR* genotype alone or combined with stressful life events found no association with

the risk of depression,<sup>77</sup> indicating the challenge of drawing genetic associations in mental health research.

Evidence is emerging to support the effect of serotonin transporter (*5-HTT*) gene-environment interactions on a wide range of psychiatric disorders other than depression. Recent data suggest that *5-HTT* gene polymorphisms influence the development of PTSD in trauma survivors.<sup>78,79</sup> Polymorphisms in *5-HTT* have also been implicated in the development of anxiety and somatic symptoms in victims of childhood sexual abuse.<sup>80</sup> These studies strengthen the traditional hypothesis that the serotonin pathway plays a common role in the development of several psychiatric disorders.

Other studies have shown that genes involved in the hypothalamic-pituitary-adrenal axis are involved in the development of psychiatric disorders such as depression and PTSD. Genetic variants in the corticotropin-releasing hormone receptor (*CRHR1*) gene polymorphisms were found to both predict and protect for the development of depression in persons with a history of trauma.<sup>81</sup> Another study found that the FK506 binding protein (*FKBP5*) polymorphisms were associated with adult PTSD symptoms in patients with a history of childhood abuse, although interestingly, *CRHR1* polymorphisms were not found to be associated with PTSD in the same population.<sup>82</sup>

As aforementioned, early evidence suggests that sexual abuse may potentiate the development of psychiatric disorders in genetically vulnerable individuals. Further research regarding this gene-environment interaction is necessary to identify which genes play a role in the development of specific psychiatric disorders and what stressful life events play a role.

Building greater awareness of the association between a history of sexual abuse and multiple psychiatric disorders will, it is hoped, lead to improved treatment and outcomes for survivors of sexual abuse. Studies have shown that survivors of sexual abuse use more medical care and incur greater costs than the general patient population. Health statistics show that abuse survivors incur 10% to 40% greater primary care costs and 13% to 43% greater total health care costs.<sup>83-87</sup> Greater health care use reflects increased emergency department visits; greater number of hospitalizations; and more generalist, subspecialty, and psychiatric evaluations.<sup>85,86,88-91</sup> Despite this increased health care use, the topic of abuse is seldom addressed between patient and physician. Only 5% of sexual abuse survivors report a history of abuse to their physicians.<sup>92</sup> Studies demonstrate that patients consider it appropriate for physicians to inquire about abuse history, but such questions are not routinely asked.<sup>93</sup>

Early evidence suggests that heightened awareness of the association between sexual abuse and mental health disorders may improve health outcomes for abuse survivors.

Both group therapy and individual psychotherapy have been shown to improve psychological symptoms among sexual abuse survivors.<sup>94-98</sup> A recent systematic review found that disclosure of childhood sexual abuse during psychotherapy may improve PTSD symptoms.<sup>99</sup> Cognitive behavioral therapy and cognitive processing therapy have also been found to be effective in treating PTSD in survivors of sexual abuse.<sup>100,101</sup> Furthermore, a recently published study demonstrated the efficacy of cognitive behavioral therapy in reducing symptoms of depression, anxiety, and PTSD in sexually abused girls.<sup>102</sup> Given the evidence for the high prevalence of sexual abuse, its association with mental health disorders, and available psychotherapeutic options, we encourage physicians to routinely inquire about sexual abuse history in patients with psychiatric symptoms. We speculate that greater awareness of the link between sexual abuse and mental health disorders will prompt earlier and more effective treatment strategies.

## CONCLUSION

Survivors of sexual abuse are commonly encountered in general medical practice. It is now known that sexual abuse survivors face a challenging spectrum of physical and mental health concerns, with associated higher health care use and greater medical expenditures. This systematic review and meta-analysis demonstrates that sexual abuse is associated with multiple psychiatric disorders, including lifetime diagnosis of anxiety disorders, depression, eating disorders, PTSD, sleep disorders, and attempted suicide. Improved recognition of the link between a history of sexual abuse and mental health disorders may increase the identification of abuse survivors and lead to better treatment and outcomes. Further research is necessary to better understand the pathogenesis of psychiatric disease in victims of sexual abuse and to more effectively treat survivors coping with long-term mental health outcomes.

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